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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,041	04/02/2001	Ralf-Christian Schlothauer	DAIRY64.001A	6853
20995	7590	11/21/2003	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP			PRATS, FRANCISCO CHANDLER	
2040 MAIN STREET			ART UNIT	
FOURTEENTH FLOOR			PAPER NUMBER	
IRVINE, CA 92614			1651	

DATE MAILED: 11/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/720,041

Applicant(s)

SCHLOTHAUER ET AL.

Examiner

Francisco C Prats

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-36, 39-50, 59 and 62-68 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 59 is/are allowed.
- 6) ☒ Claim(s) 32-36, 39-50 and 62-68 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 28, 2003, has been entered.

The amendment filed August 28, 2003, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 32-36, 39-50, 59 and 62-68 are pending and are examined on the merits.

Claim Rejections - 35 USC § 112

Claim 66 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 66 recites the additional step of testing the whey hydrolysate for "bio-activity." This new claim language

encompasses testing for many biological activities, for example anti-AIDS activity, which are clearly not supported by the disclosure as filed. Rather, the only "bioactivities" disclosed in the specification as filed are angiotensin converting enzyme inhibition and a taste test for bitterness. This is a new matter rejection.

All of applicant's argument on this issue has been full considered but is not persuasive of error. While applicant urges that the amendment of August 28, 2003, obviates this ground of rejection, note that claim 66 continues to encompass assays neither disclosed nor contemplated by the as-filed disclosure.

Claim Rejections - 35 USC § 102

Claims 32, 33, 35, 42, 44, 45, 50 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Mullally et al (Int. Dairy Journal 7:299-303 (1997)).

Mullally discloses a process whereby whey protein concentrate containing 4.7% lactose (see page 300, paragraph entitled "Substrates") is contacted with protease at a temperature of 50 degrees C at a pH of 8 to a degree of hydrolysis ranging from 0 to 8% (see Fig. 1, page 301), followed by heat inactivation of the enzyme (see page 300, paragraph

entitled "Pilot-scale hydrolysis of WPC"), followed by assaying of ACE inhibitory activity (see, e.g., Fig. 1, page 301). Mullally also processes the resulting hydrolysate by ultrafiltration with a 10 kD cutoff membrane. See, e.g., Table 2 on page 302. Mullally therefore anticipates the cited claims.

Lastly, note that Mullally is considered to anticipate claim 50 because the same substrate as claimed is contacted with the same enzyme as claimed under the same conditions as claimed to make a product having the same degree of hydrolysis as recited in the claims. The resulting product must therefore be the same. If there is a difference between the prior art and the claims, it must be due to some aspect of the process not recited in applicant's claims.

Claim Rejections - 35 USC § 103

Claims 32-36, 39-45, 50 and 62-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullally et al (Int. Dairy Journal 7:299-303 (1997)) in view of Abubakar et al (Tohoku Journal of Agricultural Research 47(1-2):1-8 (1996)).

As discussed above, Mullally discloses a process whereby the whey protein concentrate is hydrolyzed by proteases and the resulting hydrolysate is tested for ACE inhibiting activity. Mullally differs from the claims in failing to use the claimed

proteases. See applicant's claim 34. However, in view of the combined disclosures of Mullally and Abubakar, demonstrating that a large variety of proteases having different specificities all result in the production of ACE-inhibiting peptides from whey protein, the claimed use of commercially available proteases must be considered obvious under § 103(a).

Further still, the determination of suitable parameters for heat and/or pH-based enzyme inactivations (applicants' claims 36, 39 and 40) for the processes of Mullally and Abubakar would have been obvious in view of the fact that such methods of enzyme inactivation are notoriously well known in the enzymology arts, the determination of suitable or effective parameters in such processes being routinely optimized by those skilled in the art. Still further, the use of immobilized enzymes (applicant's claims 42-44) is well known in the art, and would have been obvious in view of the disclosures of Mullally and Abubakar.

Further still, the use of the hydrolysates of Mullally in the treatment of hypertension, encompassed by claim 62, clearly would have been obvious in view of the disclosure of both Mullally and Abubakar that protease-hydrolyzed whey hydrolysates possess ACE-inhibiting peptides. Still further, although neither Abubakar nor Mullally disclose the use of chromatography in the separation of peptides (applicant's claims 64-67),

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Mullally clearly discloses that using filtration to fractionate the hydrolysates on a molecular weight basis filtration results in fractions having differing, and in some cases increased, anti-hypertensive activity. Thus, Mullally clearly discloses the desirability of fractionating protease-digested whey on a molecular weight basis. The artisan of ordinary skill, recognizing at the time of applicant's invention that high performance liquid chromatography (HPLC) was a well known method of fractionating protein mixtures on the basis of molecular weight, clearly would have considered HPLC a suitable method of separating Mellqvist's whey hydrolysate on a molecular weight basis, so as to isolate those peptide fractions containing increased anti-hypertensive activity, said fractionation being taught by Mullally as being advantageous. A holding of obviousness over the cited claims is therefore required.

Claims 32-36, 39-50 and 62-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullally et al (Int. Dairy Journal 7:299-303 (1997)) in view of Abubakar et al (Tohoku Journal of Agricultural Research 47(1-2):1-8 (1996)), and in further view of Soehnlen (U.S. Pat. 4,358,464).

As discussed above, Mullally viewed in light of Abubakar renders obvious the process recited in claim 32, as recited in

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embodiments present in certain dependent claims. Mullally and Abubakar differ from the claims in that those references do not disclose the use of β -galactosidase in treating the whey product, as recited in claims 45 and 49. However, Soehnlén discloses that the use of β -galactosidase in treating a whey product, improves the taste of the product. See abstract. Thus, the artisan of ordinary skill, recognizing from Soehnlén that β -galactosidase was useful as a method of removing undesired lactose from the whey starting material or peptides resulting from the processes of Mullally and Abubakar, clearly would have been motivated to have used β -galactosidase in Mullally and Abubakar's processes to further improve the purity of the resulting product. Claim 49 must therefore be considered obvious over the cited references.

Response to Arguments

All of applicant's argument has been fully considered but is not persuasive of error. While applicant's remarks filed August 28, 2003, were not directed to the precise grounds of rejection set forth herein, all relevant argument has been fully considered. It is noted at the outset, as discussed above, that applicant's amendments have placed the Mullally reference squarely within the subject matter prescribed by the claims.

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Applicant argues that Mullally is not applicable to the claims as presently amended because Mullally teaches processes in which protease activity is stopped by heating to high temperature for an extended period of time. Applicant urges that such methods would result in changes in the conformations of the proteins and peptides in the hydrolysate, producing a hydrolysate having insoluble proteins and a modified activity. Response of August 28, 2003, page 11. Applicant urges that Mullally does not disclose a process having the same activity as a process which does not change the conformation of the proteins in the hydrolysate.

Applicant's argument ignores both the disclosure of the reference as well as the breadth of the claims under examination. At their broadest, applicant's claims do not recite any limitation regarding the duration of the heat inactivation step. Only claim 36 recites a limitation regarding the duration of the heat inactivation step. Thus, applicant's argument regarding the extended period of protease inactivation disclosed by Mullally is essentially irrelevant to every claim pending, except claim 36. With respect to claim 36, applicant's argument is factually incorrect, as clearly evidenced by the fact that both Mullally and Abubakar disclose that ACE-inhibiting peptides can be produced using precisely the

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"extended period of time" applicant urges as resulting in inactivation of the ACE-inhibiting whey-derived peptides. Moreover, both Mullally and Abubakar disclose the production of soluble products, as evidenced by Mullally's ability to filter her product.

Lastly, note that no pending claim recites anything about protein or peptide conformation. Therefore, to the extent that applicant argues such limitations, applicant is not speaking to a limitation present in the claims. Moreover, applicant has not provided any direct evidence that the peptides made by either Mullally's or Abubakar's processes are of any particular conformation.

In sum, the cited references either disclose or suggest the claimed subject matter. The anticipation and/or obviousness rejections of record are therefore clearly required.

Claim 59 is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Francisco C Prats
Primary Examiner
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FCP